VERTEX®

THE SCIENCE *of* POSSIBILITY

J.P. Morgan Healthcare Conference

January 9, 2017

Jeffrey Leiden, M.D., Ph.D.

Chairman, President and Chief Executive Officer

Safe Harbor Statement

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, (i) information pertaining to KALYDECO and ORKAMBI and the ongoing discovery, development and commercialization of Vertex's product candidates, (ii) information provided in the section captioned "Financial Profile," including preliminary financial information for the year ended December 31, 2016 and guidance for 2017 and (iii) the timing and outcome of regulatory applications, including MAAs. While the Company believes that these forward-looking statements are accurate, these statements are subject to risks and uncertainties that could cause actual outcomes to differ materially from the Company's current expectations. These risks and uncertainties include, among other things, that the Company's 2016 financial results are preliminary and subject to adjustment, that the company's expectations regarding its 2017 revenues and expenses may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), risks related to commercialization of and reimbursement for KALYDECO and ORKAMBI, the risk that data from the Company's development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, and the risks and uncertainties listed in the Company's October 25, 2016 press release and under Risk Factors in the Company's 10-K and other filings with the SEC.

Key 2016 Milestones and Goals

	2016	2017
CYSTIC FIBROSIS	✓ ORKAMBI approval and launch for ages 6-11 in the U.S.	○ Phase 3 tezacaftor/ivacaftor data in multiple mutations (1H17)
	✓ Long-term rate of lung function decline data for ORKAMBI	○ Phase 2 proof-of-concept data for two triple combination regimens in CF patients (2H17)
	✓ Phase 2 development for one or more next-generation correctors	○ Phase 1 data for for VX-659 triple combination in CF patients (2H17)
	○ Approval for KALYDECO in residual function mutations	○ Clinical development of a 4th next-generation corrector (Q117)
FINANCIAL	✓ Total CF product revenues of $1.68B, up from $983M in 2015	○ Total CF revenues of $1.79 - $2.01B
	✓ KALYDECO guidance of $670 - $690M	○ Obtain reimbursement for ORKAMBI in multiple countries outside the U.S.
	○ ORKAMBI guidance of $1.0 - $1.1B	○ Non-GAAP combined R&D and SG&A expenses of $1.25 - $1.3B
	✓ Year-end cash balance of $1.43B	
PIPELINE	✓ Bolster the CF and non-CF pipeline with internal and external assets	○ Bolster the CF and non-CF pipeline with internal and external assets
		○ Advance one or more compounds from research into clinical development

Growing Our Business in 2017 and Beyond

Cystic Fibrosis

Developing Medicines to Treat Potentially All People with the Disease

Financial Profile

Significant Revenue and Earnings Growth

Research Productivity and Strategy

Discovering and Developing Medicines to Treat Other Serious Diseases

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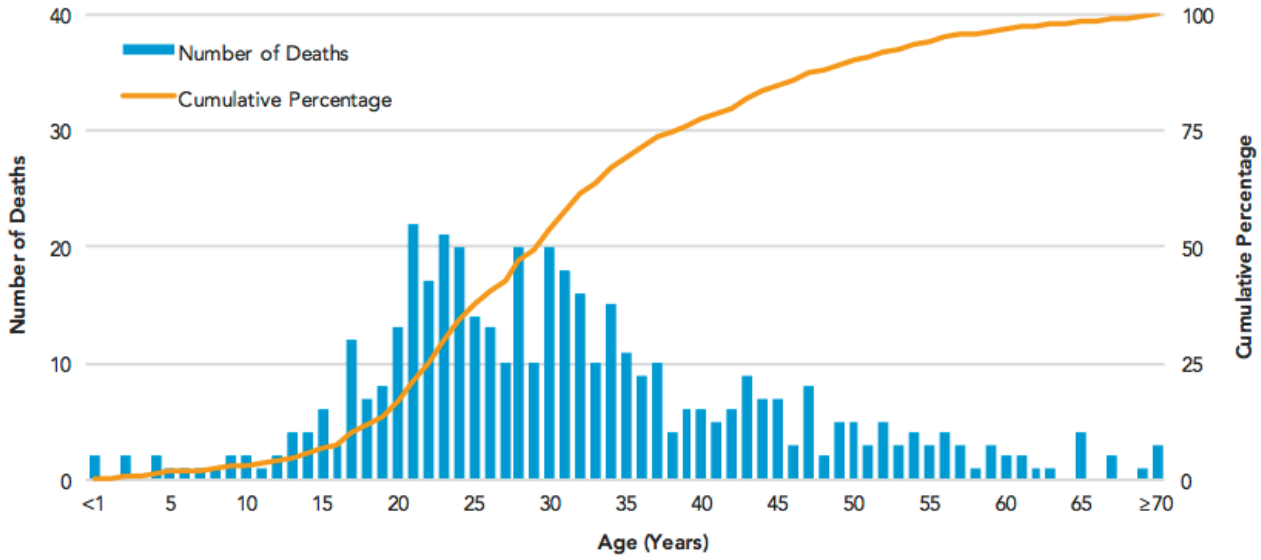
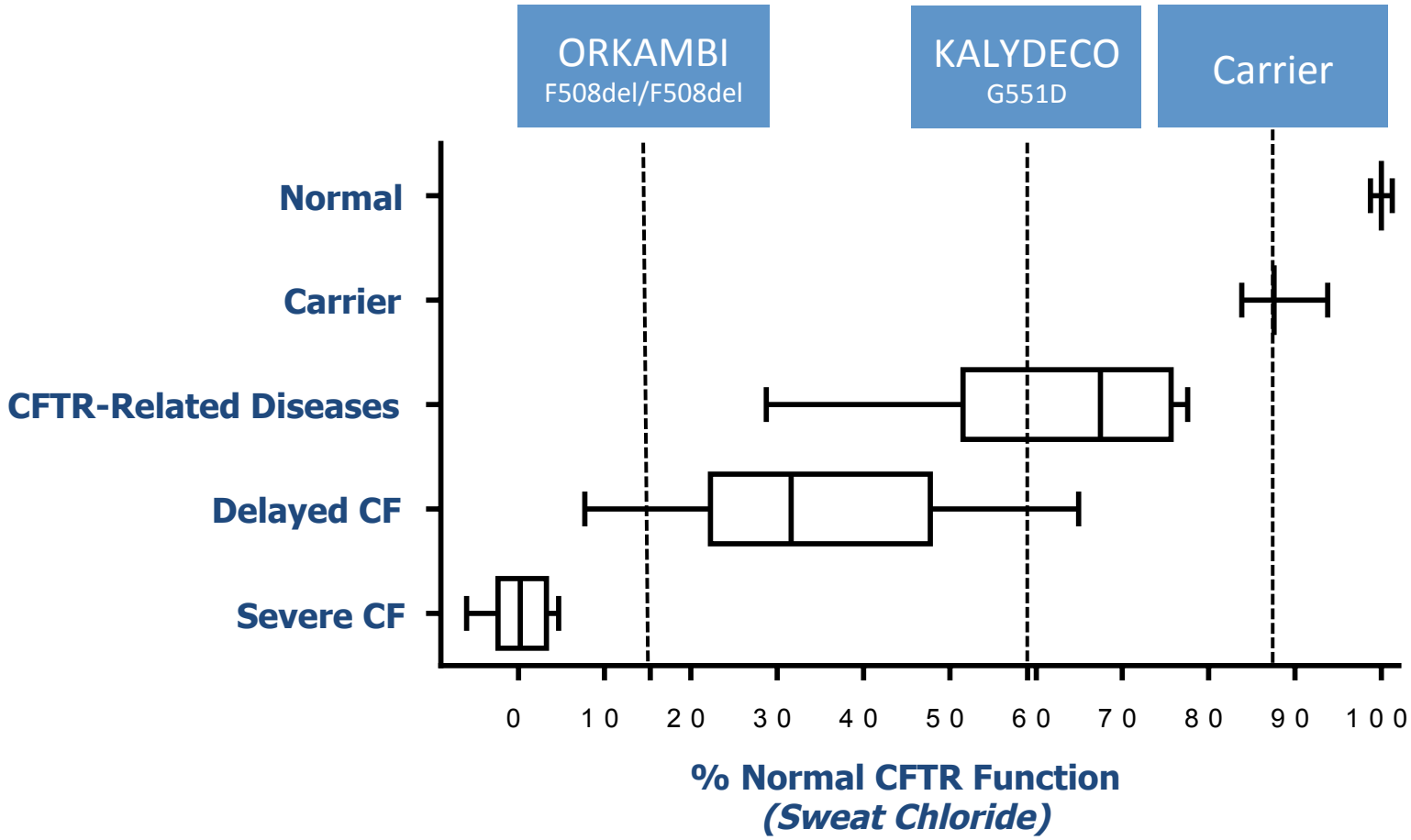
Cystic Fibrosis

- Rare, life-shortening, inherited disease caused by recessive mutations in the *CFTR* gene
- **75,000 people** in North America, Europe and Australia
- Results in thick sticky mucus that obstructs the airways, intestine & ducts of the pancreas
- Median age at death in 2015 was 30 years
- Prior to 2012, treatments only addressed symptoms, not underlying cause of disease

AGE AT DEATH IN 2015



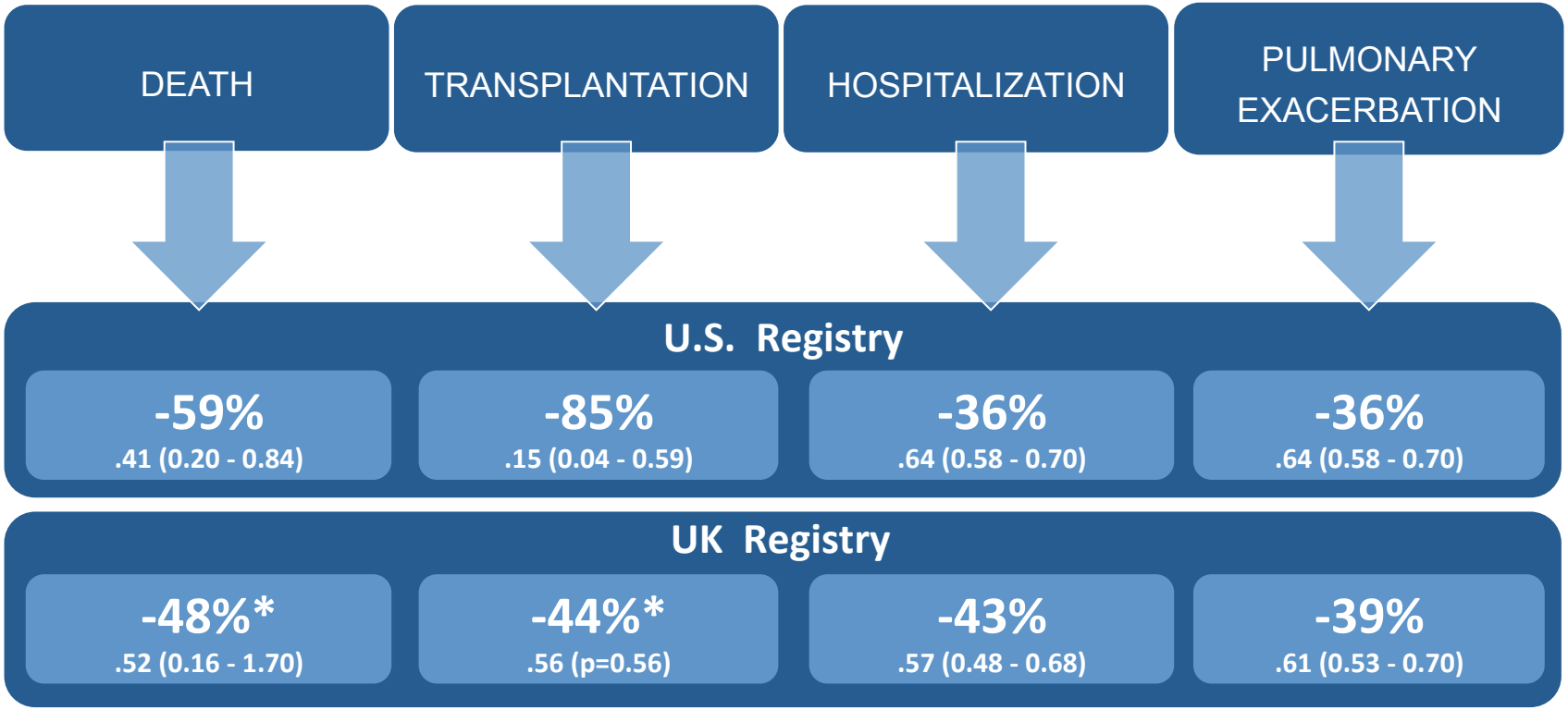
Goal: Carrier-like Benefits for All Patients Early in Life



CFTR2 Database. https://cftr2.org/. Accessed October 2016.
Riordan JR, et al. *Science.* 1989;245:1066-73; Accurso FJ, et al. *J Cyst Fibros.* 2014;13:139-47;
Boyle MP, et al. *Lancet Respir Med.* 2014;2:527-38; Ramsey BW, et al. *N Engl J Med.* 2011;365:1663-72.

Long-Term Real-World Data for KALYDECO

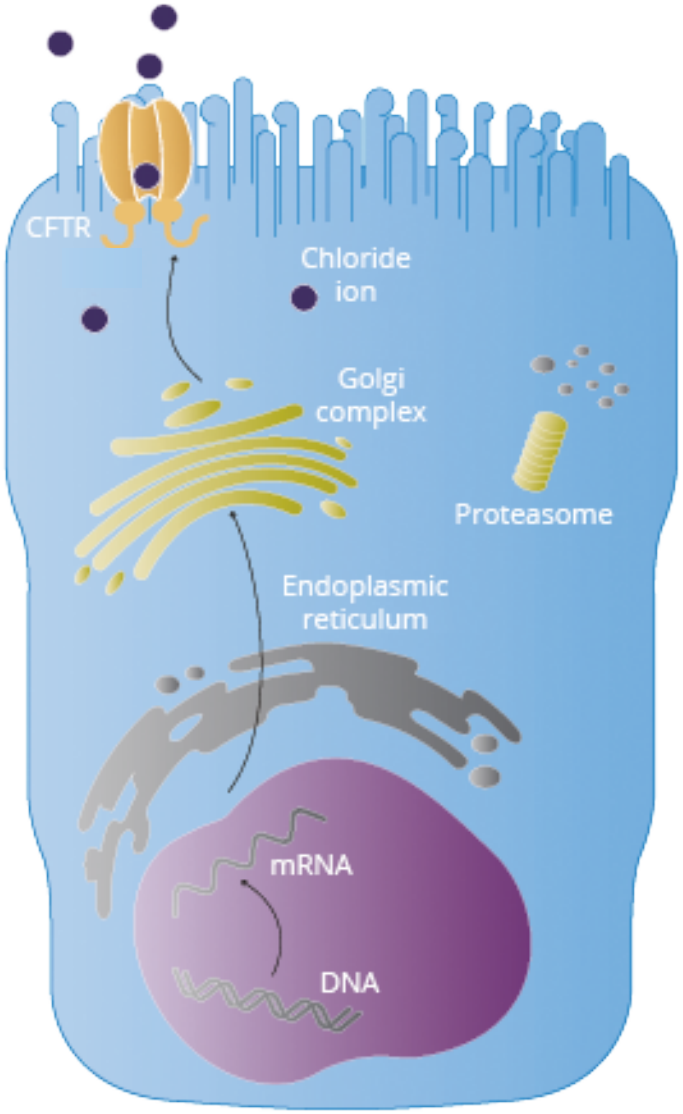
Interim data from long-term observational safety study using U.S. and UK CF Registries Presented at NACFC



Provided as Percent Reduction with corresponding Risk Ratio (95% CI); *Not Statistically Significant
Average KALYDECO exposure: 2.0 years in U.S. registry and 1.3 years in UK registry;
Potential for confounding cannot be excluded but was partially addressed through matching and stratification

Bessonova et al. Presented at 30th Annual North American Cystic Fibrosis Conference

Biological Understanding of CF Provides Path to Develop Medicines for All Patients

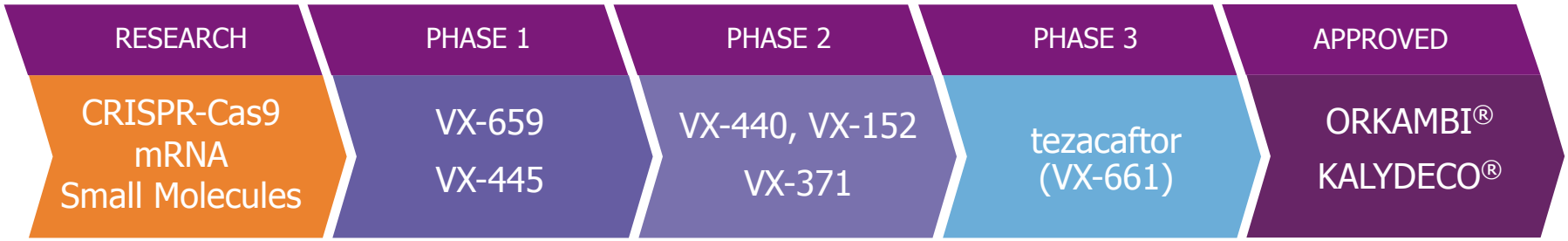


BIOLOGICAL PROBLEM	THERAPEUTIC APPROACH
Defective CFTR Function	Potentiator kalydeco (ivacaftor) tablets 150 mg oral granules 50•75 mg
Defective CFTR Protein Trafficking and Folding	Correctors ORKAMBI® (lumacaftor/ivacaftor) 200 mg / 125 mg tablets tezacaftor (VX-661) VX-440 VX-152 VX-659 VX-445
Defective Protein Synthesis	Genetic Approaches Gene Editing (CRISPR) mRNA (Moderna) Gene Therapy

Adapted from Lukacs GL, et al. *N Engl J Med.* 2003;349:1401-04.

Tezacaftor, VX-440, VX-152, VX-659, VX-445 are investigational compounds

Vertex CF Pipeline



RESEARCH

CRISPR/Cas9

- Gene editing research collaboration

mRNA

- Research collaboration and licensing agreement to develop mRNA Therapeutics™

Small Molecules

- Additional next-gen correctors potentially increasing benefit

PHASE 1

Next-Generation Correctors:

- Phase 1 study of VX-659 ongoing
- Phase 1 study of VX-445 planned for Q1 2017

PHASE 2

Next-Generation Correctors:

- Phase 2 studies of VX-440 and VX-152 ongoing

ENaC:

- Phase 2 study of VX-371 in combination with ORKAMBI ongoing

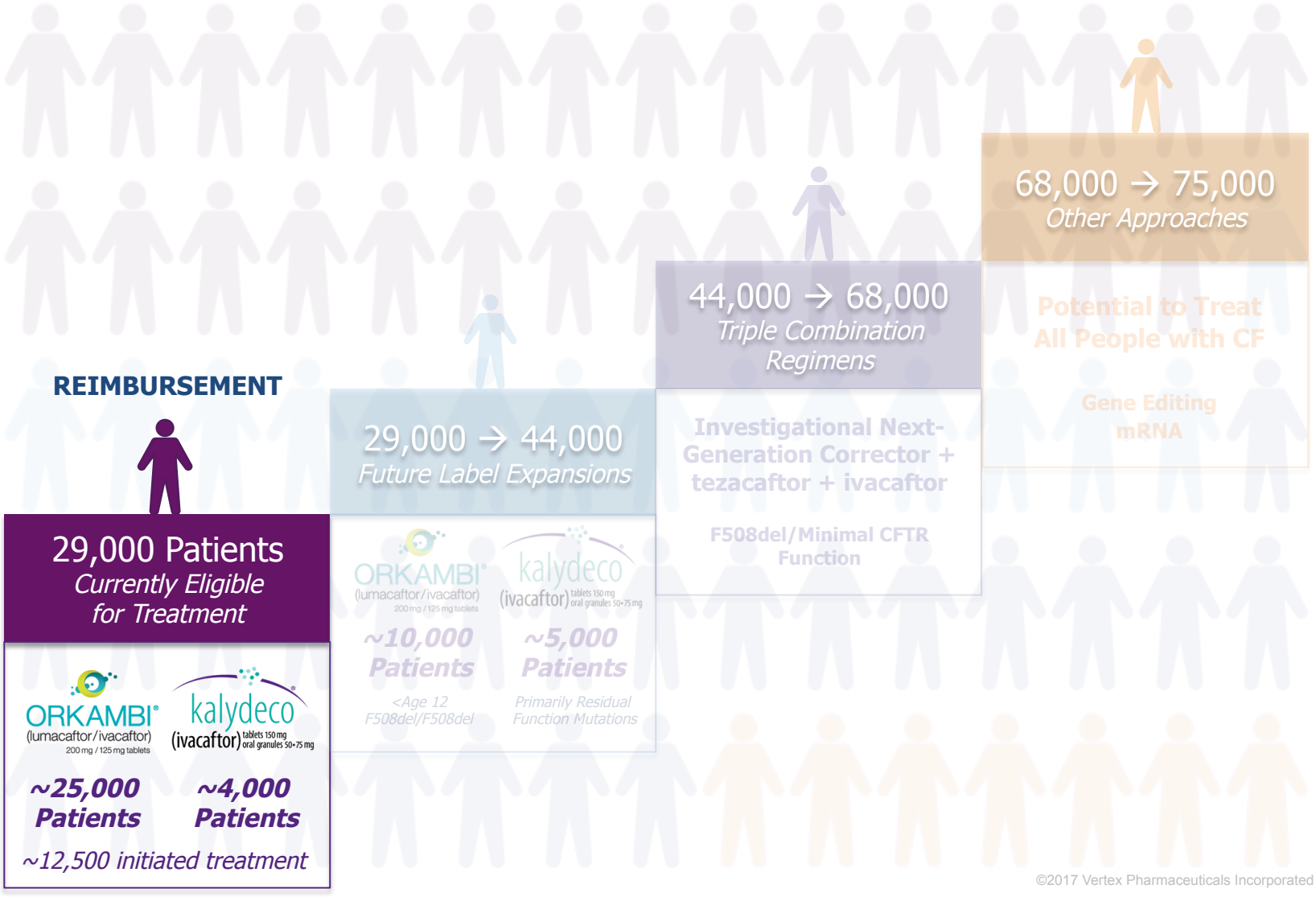
PHASE 3

- Ongoing broad Phase 3 program
- Key role in development of triple combination regimen

APPROVED

- First medicines to treat the cause of CF for people with specific mutations in the CFTR gene

Path to Treating All Patients



Growth for ORKAMBI

Increasing the Number of Eligible Patients Treated

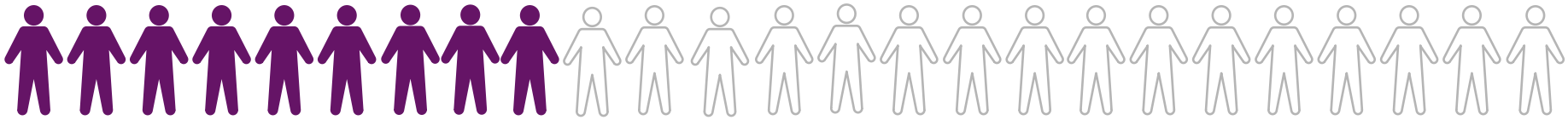
~25,000 Patients Eligible for Treatment with ORKAMBI in US, Europe, Australia and Canada

Initiated ORKAMBI

~9,000 Patients

Not Initiated ORKAMBI

~16,000 Patients



~13,000 Patients Outside the U.S., Primarily Those Awaiting Formal Reimbursement Approvals

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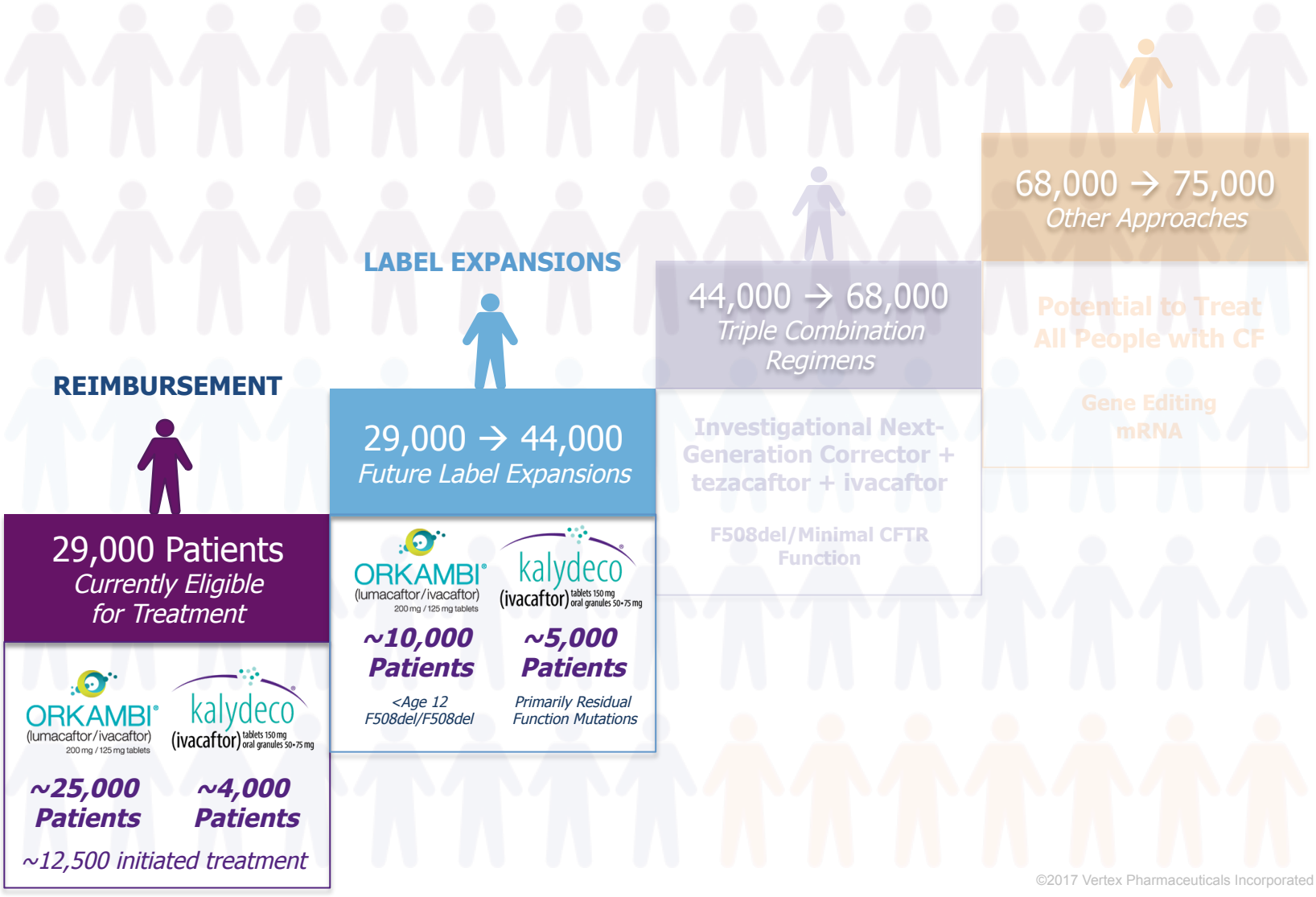
Path to Treating All Patients



Increasing the Number of Eligible Patients
ORKAMBI and KALYDECO

Label expansions could increase eligible patients from 29,000 to 44,000

ORKAMBI® (lumacaftor/ivacaftor) 200 mg / 125 mg tablets

Potential to treat ~10,000 additional children <12 years of age
(ages <6 U.S. and <12 Europe)

- Data from Phase 3 efficacy and safety study to support potential MAA approval in ages 6-11
- Phase 3 study in children ages 2-5 ongoing

kalydeco® (ivacaftor) tablets 150 mg oral granules 50•75 mg

Potential to treat ~5,000 additional people with residual function mutations and also children <2 years of age

- Phase 3 study in infants ages 0-2 ongoing
- Continue to pursue FDA approval for certain residual function mutations

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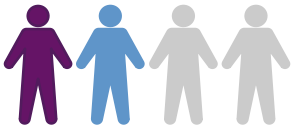
Tezacaftor (VX-661) + Ivacaftor

Broad Phase 3 Development Program



KEY GOALS

1

Evaluate the potential for a treatment option with an **enhanced benefit/risk profile** for patients with two copies of the F508del mutation

2

Evaluate the potential to **enhance benefit of KALYDECO monotherapy** in patients with one copy of the F508del mutation and a second mutation likely to respond to ivacaftor

3

Play a key role in development of **triple combination** regimens with a next-generation corrector

Phase 3 Program Generates Safety and Efficacy Data in 1,000+ Patients

First Data Expected in First Half of 2017; NDA Planned Second Half of 2017

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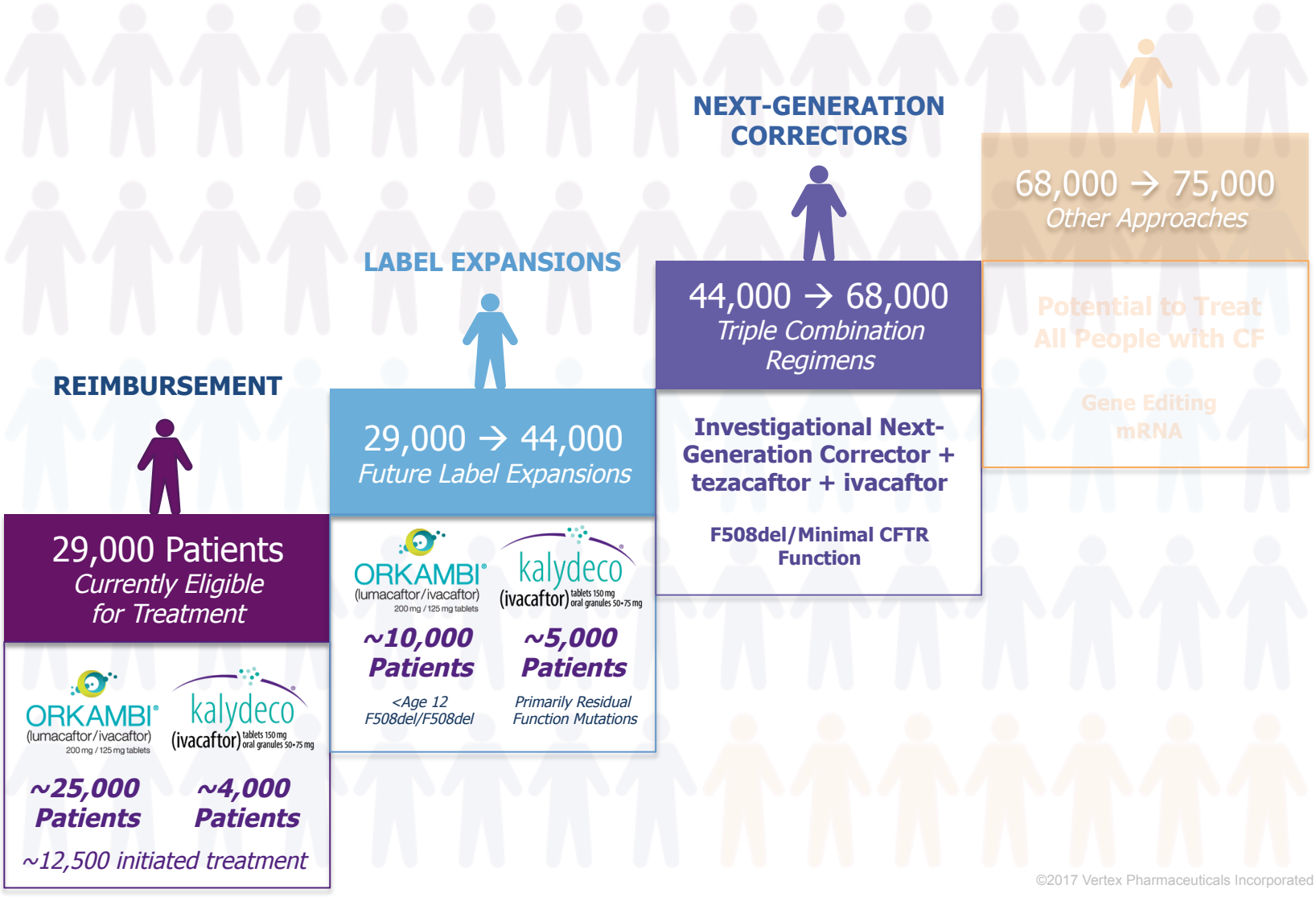
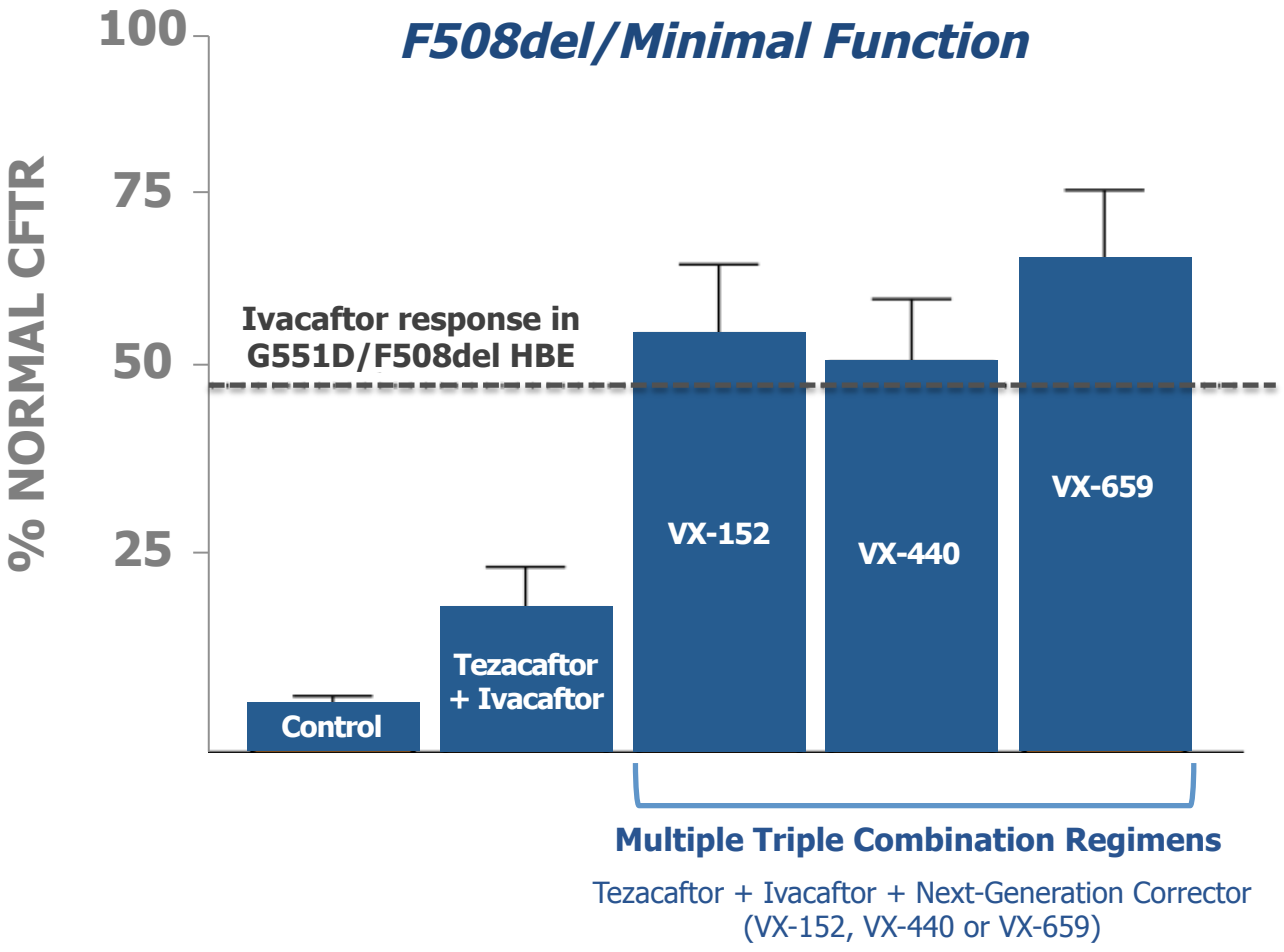
Path to Treating All Patients



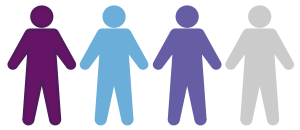
High Maximal In Vitro Efficacy for Multiple Next-Generation Correctors



N = 4 donors (2 G542X; 1 3905InsT; 1 E585X); 96-well Ussing + 20% serum; Top of bar charts represent EC 90 concentrations

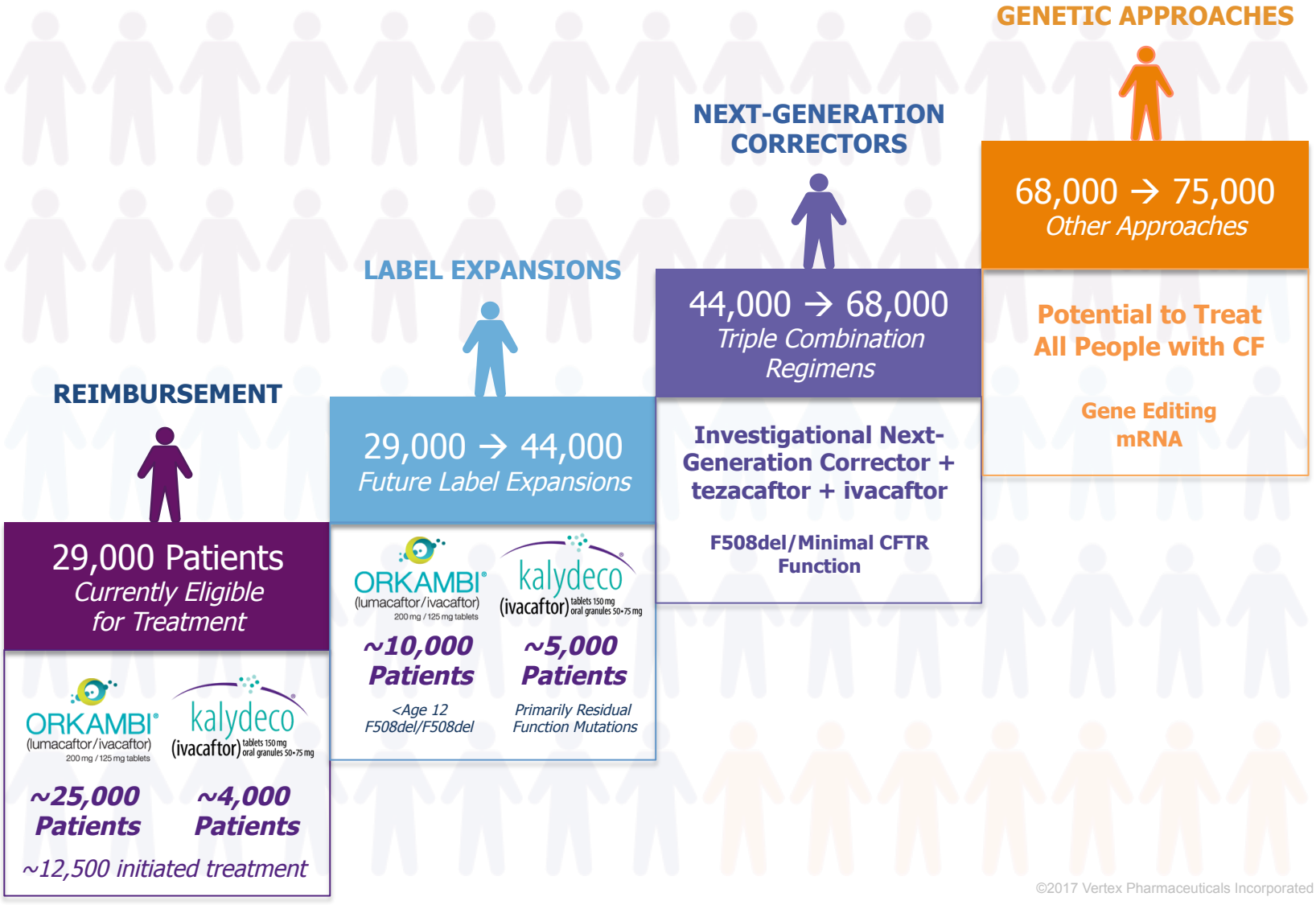
Van Goor F, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Symposium S14.4.

Broad Portfolio of Next-Generation Correctors



	RESEARCH	CLINICAL DEVELOPMENT			APPROVED
		Ph. 1	Ph. 2	Ph. 3	
VX-440 *(Fast Track Designation)*	Ph. 2 Data 2H17				***Data expected in 2H17*** *from* ***three triple combination regimens*** *in* ***CF patients***
VX-152 *(Fast Track Designation)*	Ph. 2 Data 2H17				
VX-659	Ph. 1 Data 2H17				
VX-445	Ph. 1 Planned Q117				
Additional Next-Generation Correctors					

Path to Treating All Patients



Genetic Approaches to Treat CF

CRISPR Collaboration

- Four-year research collaboration
- Initial focus:
  - Cystic Fibrosis
  - Sickle Cell Disease/Hemoglobinopathy
- Deal provides for option for exclusive licenses for up to 6 gene-based treatments

Moderna Collaboration

- Three-year research collaboration
- Focused on the use of mRNA therapies to treat the underlying cause of CF
  - Enable cells in the lungs to produce functional copies of the CFTR protein

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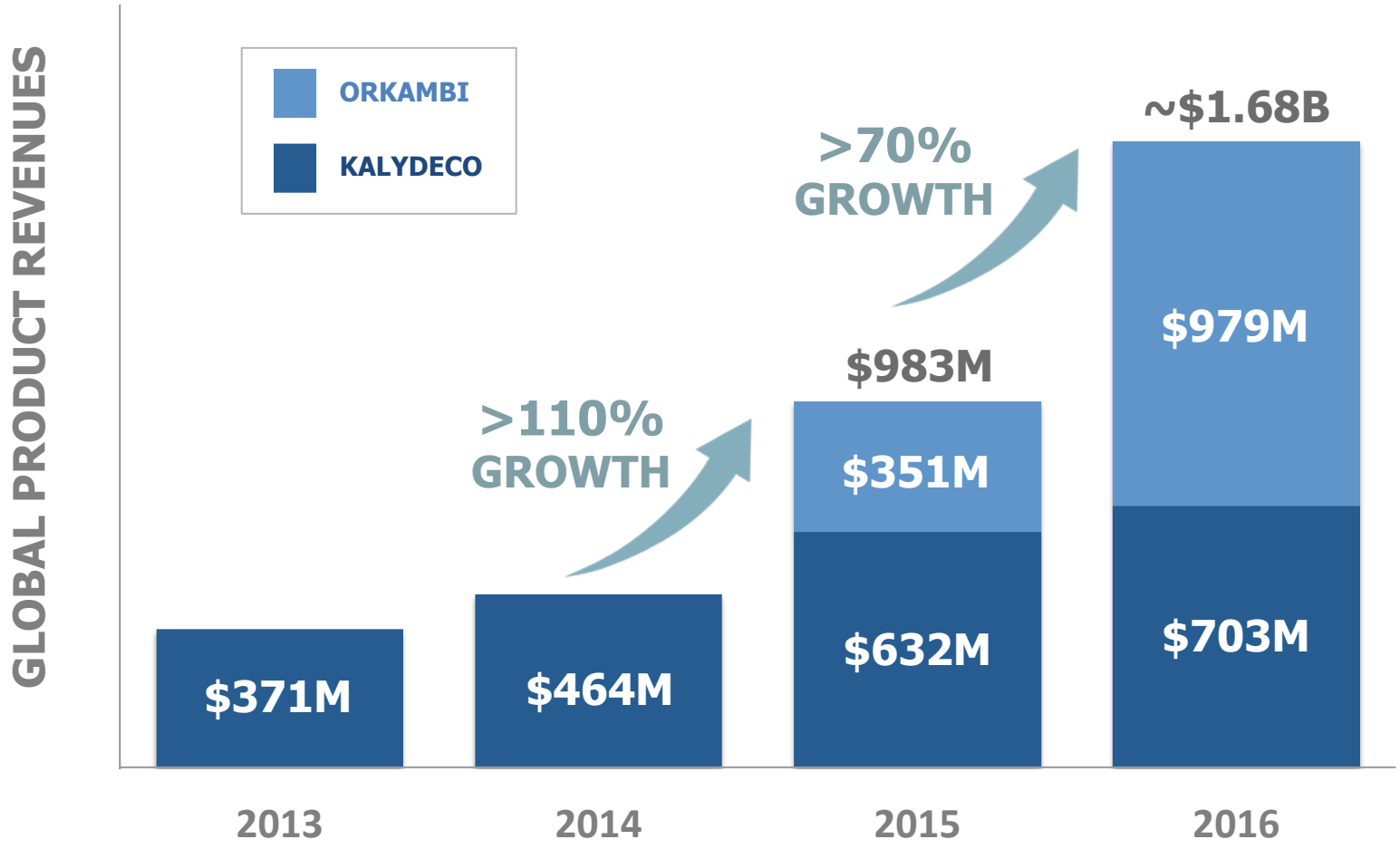
Continued Revenue Growth with Launch of ORKAMBI



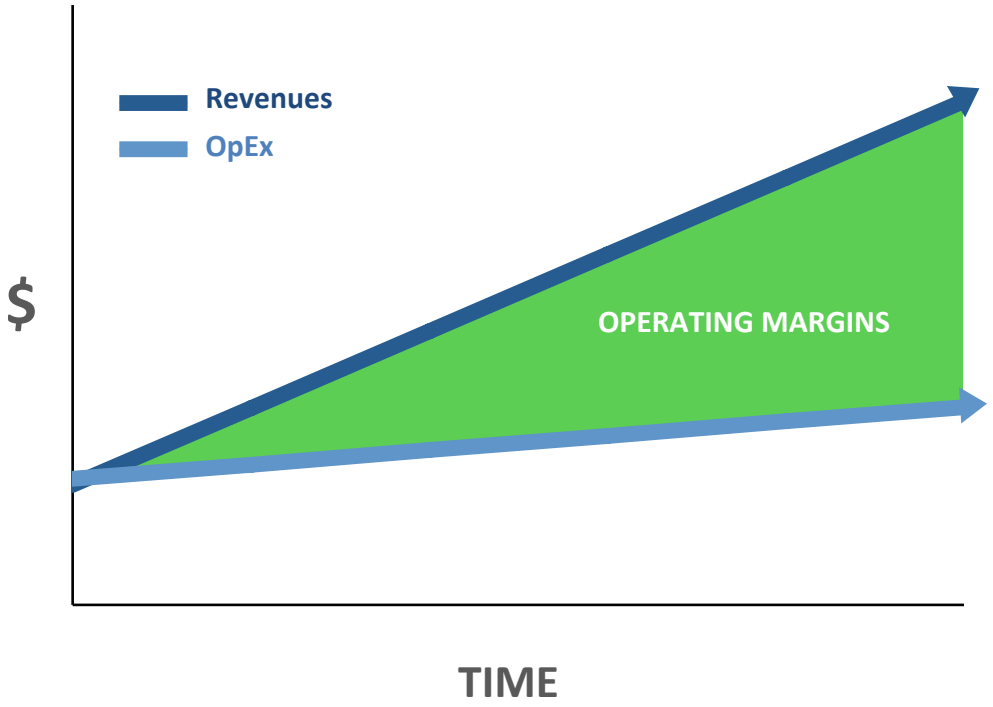
Key 2016 Financial Metrics and 2017 Guidance

	2015	2016 Preliminary Results*	2017 Guidance
ORKAMBI Revenues	$351M	$979M	$1.1 – $1.3B
KALYDECO Revenues	$632M	$703M	$690 - $710M
Total CF Revenues	$983M	$1.68B	$1.79 - $2.01B
Non-GAAP Combined R&D and SG&A Expense	$1.06B	$1.21B	$1.25 - $1.30B
GAAP Combined R&D and SG&A Expense	$1.37B	$1.48B	TBA
Cash, cash equivalents & marketable securities (year-end)	$1.04B	$1.43B	N/A

An explanation of our Non-GAAP financial measures and reconciliation of our preliminary Non-GAAP combined R&D and SG&A expense is included in our January 8, 2017 press release.
* The 2016 preliminary financial results are unaudited and are provided as approximations in advance of the company's complete financial results announcement on January 25, 2017.

CF Expansion Drives Sustainable Revenue and Earnings Growth & Enables Investment in Pipeline Assets

CF Execution & Value Creation Beyond CF



Anticipated Profile Moving Forward

- Significant revenues from multiple high-value medicines
- Modest growth in operating expenses, enabling operating margin expansion
- Continued investment in CF and non-CF pipeline
- Strengthening balance sheet

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Learnings in CF Have Transformed Our Investments in Early Research

Vertex invests in scientific innovation to create transformative medicines for specialty diseases.

RESEARCH PRINCIPLES

- **Focus** on validated targets that address causal human biology
- **Create** lab assays and clinical biomarkers to predict clinical response
- **Discover and develop** medicines that offer transformative benefit
- **Identify** rapid path to registration and beyond

DISEASES CURRENTLY BEING TARGETED IN VERTEX RESEARCH

- **Adrenoleukodystrophy (ALD)**
- **Alpha-1 Antitrypsin Deficiency (AATD)**
- **Sickle Cell Disease & Beta Thalassemia**
- **Polycystic Kidney Disease**

Alpha-1 Antitrypsin Deficiency (AATD)

DISEASE

- Genetic disorder caused by a single point mutation in the SERPINA1 gene that causes a protein folding defect
- Causes lung & liver disease; 60,000 patients in the U.S.

CURRENT TREATMENT

- 10,000 patients currently treated
- Current replacement therapy only partially effective

CONSISTENT WITH VERTEX STRATEGY

- ✓ Validated target
- ✓ Predictive lab assays
- ✓ Potential for transformative benefit
- ✓ Rapid proof of concept

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Key 2017 Milestones and Goals

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